Paper 21

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOACHIM GOEDE, HELMUT HETTCHE,
HELMUT MOMBERGER, JURGEN ENGEL and MICHAEL LOBISCH

Appeal 1997-3391
Application 08/212,578[1]

Before: WINTERS and WILLIAM F. SMITH, Administrative Patent Judges, and McKELVEY, Senior Administrative Patent Judge.

McKELVEY, Senior Administrative Patent Judge.

MEMORANDUM OPINION and ORDER
Decision on appeal under 35 U.S.C. § 134

The appeal is from a decision of the Primary Examiner, entered for the first time in the Examiner's Answer, rejecting claims 1-7. We affirm.

A. Findings of fact

The record supports the following findings by a preponderance of the evidence.

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[1] Application for patent filed 17 March 1994. Applicants claim priority under 35 U.S.C. § 119 of German patent application P 43 08 572.5, filed 18 March 1993 and German patent application P 43 19 649.7, filed 14 June 1993. The real party in interest is believed to be Asta Medica AG.

The claims

1. The claims on appeal are claims 1-7.

2. According to applicants' reply brief, the claims stand or fall together (page 1).

3. Claim 1 reads as following (indentation and paragraph numbering added):

> A pharmaceutical dosage unit comprising:
>
> [1] flupirtine, its pharmaceutically acceptable salts or mixtures thereof and
>
> [2] a controlled-release component,
>
> wherein 0.001 to 20 parts controlled release component are present for each part by weight flupirtine (calculated as flupirtine base)
>
> which results in a release rate of flupirtine between 5 and 300 mg per hour, determined in accordance with the method of USP XXII with apparatus 2 in an aqueous test solution of pH 1.0 and/or pH 6.8.

The invention

4. Flupirtine is a known pharmaceutical useful as an analgesic (specification, page 1, line 12).

5. According to applicants, its use "sometimes causes a sedative side-effect" (specification, page 1, lines 12-13).

6. An object of applicants' invention is to provide a solid dosage form of flupirtine in which the sedative side

effects "are largely or totally suppressed" (specification, page 1, lines 15-18).

7. The object of the invention is said to be achieved through a pharmaceutical dosage composition containing (1) flupirtine and (2) a delayed-action or controlled-release component (specification, page 1, line 31 through page 2, line 3).

8. Flupirtine may be present per se (in the form of a base) or in the form of salt, e.g., flupirtine maleate.

9. The pharmaceutical dosage composition contains 0.001 to 20 parts by weight of delayed-action or controlled-release component per 1 part of flupirtine (calculated as base) (specification, page 2, lines 6-8).

10. The release is said to take place at the rate of 5 to 300 mg of flupirtine per hour (specification, page 2, line 9).

11. Examples 1 and 2 show compositions within the scope of the invention and describe a release rate. Examples 3 and 4 show compositions within the scope of the invention, but do not describe release rates.[2]

12. Significantly, our attention has not been called to any objective data in the specification with respect to side

[2] On the basis of the record before us, we voice no opinion on whether the examples are based on actual experimentation or are prophetic. We note that the present, as opposed to the past, tense is used in the examples.

effects, either for prior art flupirtine compounds or pharmaceutical compositions with the scope of the invention.

13. Thus, on this record all we have is applicants' assertion that side effects are reduced when the compositions of claim 1 are used as an analgesic.

The examiner's rejection

14. A final rejection was withdrawn in the Examiner's Answer, where a new ground of rejection was entered (Examiner's Answer, page 3).

15. The examiner has rejected claims 1-7 as being unpatentable under 35 U.S.C. § 103 over Lobisch, U.S. Patent 5,162,346 (1992), Tamás, U.S. Patent 4,748,023 (1988) and Eichel, U.S. Patent 5,238,686 (1993).

16. Applicants timely filed a reply brief responding to the examiner's new ground of rejection.

17. There was no further response by the examiner.

Lobisch

18. Lobisch reveals that flupirtine "is an analgesic, i.e., it causes an insensibility to pain without anesthesia or loss of consciousness" (col. 1, lines 11-15).

19. In fact, flupirtine is said to have "a pronounced analgesic effect" (col. 2, lines 23-24).

20. According to Lobisch (col. 2, lines 1-6):

> A muscle-relaxing effect was noted following the intraperitoneal administration of flupirtine in an analgesically effective dose range, no central side effects such as ataxia or reduction in spontaneous motility being observed in the animals treated with flupirtine in the dose range investigated.

21. Flupirtine apparently can be administered in a variety of forms, including "tablets, capsules, pills, coated tablets, suppositories, ointments, gels, creams, powders, dusting powders, aerosols or in liquid form" (col. 3, lines 9-12).

22. A preferred form is said to be capsules or tablets containing between 100 mg and 200 mg by weight of flupirtine (col. 3, lines 15-18).

23. According to Lobisch (col. 3, lines 28-30):

> It is for example possible to recommend 1 to 2 capsules or tablets containing 50 mg to 200 mg of active substance 3 times daily.

24. However, capsules and tablets may contain dosage units of 50 mg up to 500 mg of flupirtine (col. 4, lines 20-22).

25. The preparation of Lobisch's pharmaceutical compositions "is effected in conventional manner, it also being possible to use conventional and customary pharmaceutical auxiliary substances and other conventional carriers and diluents" (col. 5, lines 5-9).

Tamás and Eichel

26. Tamás and Eichel describe the use of pharmaceuticals in the form of sustained release compositions.

27. The Tamás invention is applicable to any active ingredient and is said to ensure a high active ingredient content (col. 2, lines 20-22).

28. Release of an active ingredient can take place within about 8 hours (col. 2, lines 41-43).

29. Tamás reveals the following about the knowledge possessed by one skilled in the art (col. 5, lines 24-31):

> In the case of certain active ingredients the parameters which ensure optimal release rate (e.g., starting particle size of the active ingredient, amount of ethyl cellulose, character and amount of the disintegrating agent, etc.) cannot be given in advance but are to be determined by experiments which belong to the obligatory knowledge of the skilled art worker and can be easily performed.

30. Eichel emphasizes a sustained-release system for aspirin (col. 1, lines 15-20).

31. With certain drugs, Eichel tells us that "repeated dosages must be taken at frequent intervals to obtain long term pain relief" (col. 1, lines 27-29).

32. By using a sustained-release system, "[e]xcess drug concentrations are minimized and steady long-term release of the drug is maximized" (col. 3, lines 43-45).

33. Eichel explicitly suggests that sustained-release systems are useful for "analgesics" other than aspirin (col. 4, lines 4-11). Flupirtine is an analgesic (Finding 4).

34. Eichel mentions 8-hour sustained release systems (col. 4, line 45) and 12-hour sustained release systems (col. 8, line 30).

B. Discussion

According to applicants, the prior art does not make out a prima facie case of obviousness. We disagree.

The use of sustained-release systems to administer drugs is well-known. There are numerous reasons recognized the art for their use. Elimination of frequent dosages (Eichel, col. 1, lines 27-29) and minimizing excess drug concentration in the body at any particular time (col. 3, lines 43-45) are benefits of a sustained-release system. Optimal absorption of a drug is also a benefit (Tamás, col. 2, lines 41-43). The benefits are applicable to the administration of analgesics (Eichel, col. 4, lines 10-11) and flupirtine is a known analgesic.

But, applicants contend that there is no reason to combine the teachings of Lobisch with sustained-release art such as

Eichel and Tamás. Again, we disagree. Lobisch suggests the administration of flupirtine over several doses during a single day. Thus, Lobisch is able to recommend 3 doses per day of a capsule or tablet having 50 mg to 200 mg of active ingredient, i.e., flupirtine (col. 3, lines 28-30). A person having ordinary skill in the art would immediately recognize the benefit of the use of a sustained-release system to spread administration of flupirtine over time while securing the advantages recognized by Eichel and Tamás.

Applicants maintain that the prior art does not suggest that side-effects, and in particular sedative side-effects, would be minimized with a sustained-release system. The CCPA has provided a complete answer to applicants' argument. In re Klosak, 455 F.2d 1077, 1080, 173 USPQ 14, 16 (CCPA 1972) (an inventor must show that the results the inventor says are obtained with the invention are actually obtained with his invention). The fatal flaw in applicants' argument is that there is no evidence in the record that administration of flupirtine with a sustained-release system avoids sedative side effects. In fact, Lobisch suggests that certain side effects were not found in certain experiments involving flupirtine (Lobisch, col. 2, lines 3-6). We do not know the basis for applicants' assertion in the specification that sedative side-effects are reduced. To the extent that the assertions in the specification are those of an "expert," we

simply respond that there is nothing in Federal Circuit jurisprudence which requires the examiner or us to accept an unsupported assertion of an expert. Rohm and Haas Co. v. Brotech Corp., 127 F.3d 1089, 1092, 44 USPQ2d 1459, 1462 (Fed. Cir. 1997). We decline, in this case, to credit the unsupported statements in applicants' specification.

Applicants rely on the proportions of flupirtine to release composition and the release rate. But, our reading of the record reveals that a person having ordinary skill in the art would have been able to determine operable, if not optimal, release rates for a particular drug (Tamás, col. 5, line 25). The mere fact that Lobisch reveals a dosage range (col. 3, lines 28-30) tells us that a person having ordinary skill in the art would have known how to determine a proper dosage. Likewise, a person having ordinary skill in the art would have been able to determine the ratio of flupirtine to release composition. Tamás reveals a high active ingredient ratio and Eichel describes a variety of drug/sustained release component ratios (col. 4, lines 12-24).

Applicants criticize Eichel because it delivers its drug in the small intestine. Curiously, applicants do not tell us how flupirtine is delivered to the body when taken orally.

The rejection is attacked on the ground that Lobisch does not attempt to solve any problem described by Eichel and Tamás

and that none of the three prior art references describe the problem (minimizing sedative side-effects) said to have been solved by applicants. Apart from the fact that there is no evidence that applicants solve any sedative problem, the reason for combining teachings of the prior art need not be the same as the reason applicants developed an invention. In re Kemps, 97 F.3d 1427, 1430, 40 USPQ2d 1309, 1311 (Fed. Cir. 1996) ("Although the motivation to combine here differs from that of the applicant, the motivation in the prior art to combine the references does not have to be identical to that of the applicant to establish obviousness.").

We have considered all other argument presented, but find them unavailing.

C. Decision

The decision of the examiner rejecting claims 1-7 under 35 U.S.C. § 103 over Lobisch, Eichel and Tamás is affirmed.

AFFIRMED.

SHERMAN D. WINTERS,)
Administrative Patent Judge)
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WILLIAM F. SMITH,) BOARD OF PATENT
Administrative Patent Judge) APPEALS AND

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